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Assistant Commissioner for Patents
Washington, D.C. 20231

On February 13, 2003

TOWNSEND and TOWNSEND and CREW LLP

By: _____

PATENT
Attorney Docket No.: 17726A-000420US

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

LEE *et al.*

Application No.: 10/028,726

Filed: December 21, 2001

For: PRODUCTS AND METHODS FOR CONTROLLING THE SUPPRESSION OF THE NEOPLASTIC PHENOTYPE

Examiner: Not yet assigned

Art Unit: 1633

COMMUNICATION UNDER

37 C.F.R. §§ 1.821-1.825

AND

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, 37 C.F.R. §§ 1.821-1.825, mailed December 13, 2002, Applicants submit that the computer-readable form in the instant application is identical with that filed in Application No. 08/472,760, filed November 27,1996. In accordance with 37 C.F.R. § 1.821(e), please use the computer-readable form filed in Application No. 08/472,760 as the computer-readable form for the instant application. A paper copy of the last filed Sequence Listing from Application No. 08/472,760 is submitted herewith. The information in the paper copy of the Sequence Listing is identical to that which is in the computer readable form, as required under 37 C.F.R. § 1.821(f).

It is understood that the Patent and Trademark Office will make the necessary changes in application number and filing date for the computer-readable form that will be used for the instant application.

Please amend the specification in adherence with 37 C.F.R. §§ 1.821-1.825 as follows.

In the Specification:

Please replace paragraph **[152]** beginning at page 27, line 15, with the following:

[152] --The hypothetical protein predicted from the nucleotide sequence was expected to have MW about 106 kD. The immunoprecipitated protein has a MW about 110-114 kD. The complete RB protein amino acid sequence (SEQ ID NO:2) is illustrated in Table 1. This complete sequence obtained from the newly reconstructed clone which contains the most 5' end stretch missing in the original cDNA clone Science, 235:1394-1399 (1987).

TABLE 1

```
        MPPKTPRKTAATAAAAAAAEPPAPPPPPPPPEEDPE    ( 34)
QDSGPEDLPLVRLEFEETEEPDFTALCQKLKIPDHVRERA    ( 74)
WLTWEKVSSVDGVLGGYIQKKKELWGICIFIAAVDLDEMS    (114)
FTFTELQKNIEISVHKFFNLLKEIDTSTKVDNAMSRLLKK    (154)
YDVLFALFSKLERTCELIYLTQPSSSISTEINSALVLKVS    (194)
WITFLLAKGEVLQMEDDLVISFQLNLCVLDYFIKLSPPML    (234)
LKEPYKTAVIPINGSPRTPRRGQMRSARIAKQLENDTRII    (274)
EVLCKEHECNIDEVKNVYFKNFIPFMNSLGLVTSNGLPEV    (314)
ENLSKRYEEIYLKNKDLDARLFLDHDKTLQTDSIDSFETQ    (354)
RTPRKSNLDEEVNVIPPHTPVRTVMNTIQQLMMILNSASD    (394)
QPSENLISYFNNCTVNPKESILKRVKDIGYIFKEKFAKAV    (434)
GQGCVEIGSQRYKLGVRLYYRVMESMLKSEEERLSIQNFS    (474)
KLLNDNIFHMSLLACALEVVMATYSRSTSQNLDSGTDLSF    (514)
PWILNVLNLKAFDFYKVIESFIKAEGNLTREMIKHLERCE    (554)
HRIMESLAWLSDSPLFDLIKQSKDREGPTDHLESACPLNL    (594)
PLQNNHTAADMYLSPVRSPKKKGSTTRVNSTANAETQATS    (634)
AFQTQKPLKSTSLSLFYKKVYRLAYLRLNTLCERLLSEHP    (674)
ELEHIIWTLFQHTLQNEYELMRDRHLDQIMMCSMYGICKV    (714)
KNIDLKFKIIVTAYKDLPHAVQETFKRVLIKEEEYDSIIV    (754)
FYNSVFMQRLKTNILQYASTRPPTLSPIPHIPRSPYKFPS    (794)
SPLRIPGGNIYISPLKSPYKISEGLPTPTKMTPRSRILVS    (834)
IGESFGTSEKFQKINQMVCNSDRVLKRSAEGSNPPKPLKK    (874)
LRFDIEGSDEADGSKHLPGESKFQQKLAEMTSTRTRMQKQ    (914)
KMNDSMDTSNKEEK                              (928)
```

single-letter abbreviations for the amino acid residues are:
A, Ala; C, Cys; D, Asp; E, Gly; F, Phe; G, Gly; H, His;
I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln;
R, Arg; S, Ser; T, Thr; V, Val; W, Trp; and Y, Tyr.--

Please replace paragraph **[153]** beginning at page 27, line 15, with the following:

[153] --The amino acid sequence (Table 1; SEQ ID NO:2) is written in the abbreviation code recognized in the art. Single-letter abbreviations for the amino acid residues are: A = Alanine, C = Cysteine, D = Aspartic acid, E = Glutamic Acid, F = Phenylalanine, G = Glycine, H = Histidine, I = Isoleucine, K = Lysine, L = Leucine, M = Methionine, N =

Asparagine, P = Proline, Q = Glutanine, R = Arginine, S = Serine, T = Threonine, V = Valine, W = Tryptophane and Y = Tyrosine.--

Please replace paragraph **[225]** beginning at page 27, line 15, with the following:

[225] --Pending U.S. patent application Serial No. 108,748 discloses and claims the RB gene and its clone. The RB gene and its clone had the nucleotide and amino acid sequences ~~sequence~~ depicted in Table 4 ~~Table 2~~ (SEQ ID NOS:1 and 2).

TABLE 4

```
TTCCGGTTTT TCTCAGGGGA CGTTGAAATT ATTTTTGTAA CGGGAGTCGG GAGAGGACGG      60

GGCGTGCCCC GCGTGCGCGC GCGTCGTCCT CCCCGGCGCT CCTCCACAGC TCGCTGGCTC     120

CCGCCGCGGA AAGGCGTC ATG CCG CCC AAA ACC CCC CGA AAA ACG GCC GCC        171
                       Met Pro Pro Lys Thr Pro Arg Lys Thr Ala Ala
                         1               5                  10

ACC GCC GCC GCT GCC GCC GCG GAA CCC CCG GCA CCG CCG CCG CCG CCC        219
Thr Ala Ala Ala Ala Ala Ala Glu Pro Pro Ala Pro Pro Pro Pro Pro
            15                  20                  25

CCT CCT GAG GAG GAC CCA GAG CAG GAC AGC GGC CCG GAG GAC CTG CCT        267
Pro Pro Glu Glu Asp Pro Glu Gln Asp Ser Gly Pro Glu Asp Leu Pro
        30                  35                  40

CTC GTC AGG CTT GAG TTT GAA GAA ACA GAA GAA CCT GAT TTT ACT GCA        315
Leu Val Arg Leu Glu Phe Glu Glu Thr Glu Glu Pro Asp Phe Thr Ala
    45                  50                  55

TTA TGT CAG AAA TTA AAG ATA CCA GAT CAT GTC AGA GAG AGA GCT TGG        363
Leu Cys Gln Lys Leu Lys Ile Pro Asp His Val Arg Glu Arg Ala Trp
60                  65                  70                  75

TTA ACT TGG GAG AAA GTT TCA TCT GTG GAT GGA GTA TTG GGA GGT TAT        411
Leu Thr Trp Glu Lys Val Ser Ser Val Asp Gly Val Leu Gly Gly Tyr
                80                  85                  90

ATT CAA AAG AAA AAG GAA CTG TGG GGA ATC TGT ATC TTT ATT GCA GCA        459
Ile Gln Lys Lys Lys Glu Leu Trp Gly Ile Cys Ile Phe Ile Ala Ala
            95                  100                 105

GTT GAC CTA GAT GAG ATG TCG TTC ACT TTT ACT GAG CTA CAG AAA AAC        507
Val Asp Leu Asp Glu Met Ser Phe Thr Phe Thr Glu Leu Gln Lys Asn
        110                 115                 120
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ATA GAA ATC AGT GTC CAT AAA TTC TTT AAC TTA CTA AAA GAA ATT GAT      555
Ile Glu Ile Ser Val His Lys Phe Phe Asn Leu Leu Lys Glu Ile Asp
    125                 130                 135

ACC AGT ACC AAA GTT GAT AAT GCT ATG TCA AGA CTG TTG AAG AAG TAT      603
Thr Ser Thr Lys Val Asp Asn Ala Met Ser Arg Leu Leu Lys Lys Tyr
140                 145                 150                 155

GAT GTA TTG TTT GCA CTC TTC AGC AAA TTG GAA AGG ACA TGT GAA CTT      651
Asp Val Leu Phe Ala Leu Phe Ser Lys Leu Glu Arg Thr Cys Glu Leu
                160                 165                 170

ATA TAT TTG ACA CAA CCC AGC AGT TCG ATA TCT ACT GAA ATA AAT TCT      699
Ile Tyr Leu Thr Gln Pro Ser Ser Ser Ile Ser Thr Glu Ile Asn Ser
            175                 180                 185

GCA TTG GTG CTA AAA GTT TCT TGG ATC ACA TTT TTA TTA GCT AAA GGG      747
Ala Leu Val Leu Lys Val Ser Trp Ile Thr Phe Leu Leu Ala Lys Gly
        190                 195                 200

GAA GTA TTA CAA ATG GAA GAT GAT CTG GTG ATT TCA TTT CAG TTA ATG      795
Glu Val Leu Gln Met Glu Asp Asp Leu Val Ile Ser Phe Gln Leu Met
    205                 210                 215

CTA TGT GTC CTT GAC TAT TTT ATT AAA CTC TCA CCT CCC ATG TTG CTC      843
Leu Cys Val Leu Asp Tyr Phe Ile Lys Leu Ser Pro Pro Met Leu Leu
220                 225                 230                 235

AAA GAA CCA TAT AAA ACA GCT GTT ATA CCC ATT AAT GGT TCA CCT CGA      891
Lys Glu Pro Tyr Lys Thr Ala Val Ile Pro Ile Asn Gly Ser Pro Arg
                240                 245                 250

ACA CCC AGG CGA GGT CAG AAC AGG AGT GCA CGG ATA GCA AAA CAA CTA      939
Thr Pro Arg Arg Gly Gln Asn Arg Ser Ala Arg Ile Ala Lys Gln Leu
            255                 260                 265

GAA AAT GAT ACA AGA ATT ATT GAA GTT CTC TGT AAA GAA CAT GAA TGT      987
Glu Asn Asp Thr Arg Ile Ile Glu Val Leu Cys Lys Glu His Glu Cys
        270                 275                 280

AAT ATA GAT GAG GTG AAA AAT GTT TAT TTC AAA AAT TTT ATA CCT TTT     1035
Asn Ile Asp Glu Val Lys Asn Val Tyr Phe Lys Asn Phe Ile Pro Phe
    285                 290                 295

ATG AAT TCT CTT GGA CTT GTA ACA TCT AAT GGA CTT CCA GAG GTT GAA     1083
Met Asn Ser Leu Gly Leu Val Thr Ser Asn Gly Leu Pro Glu Val Glu
300                 305                 310                 315

AAT CTT TCT AAA CGA TAC GAA GAA ATT TAT CTT AAA AAT AAA GAT CTA     1131
Asn Leu Ser Lys Arg Tyr Glu Glu Ile Tyr Leu Lys Asn Lys Asp Leu
                320                 325                 330
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GAT GCA AGA TTA TTT TTG GAT CAT GAT AAA ACT CTT CAG ACT GAT TCT      1179
Asp Ala Arg Leu Phe Leu Asp His Asp Lys Thr Leu Gln Thr Asp Ser
            335                 340                 345

ATA GAC AGT TTT GAA ACA CAG AGA ACA CCA CGA AAA AGT AAC CTT GAT      1227
Ile Asp Ser Phe Glu Thr Gln Arg Thr Pro Arg Lys Ser Asn Leu Asp
        350                 355                 360

GAA GAG GTG AAT GTA ATT CCT CCA CAC ACT CCA GTT AGG ACT GTT ATG      1275
Glu Glu Val Asn Val Ile Pro Pro His Thr Pro Val Arg Thr Val Met
    365                 370                 375

AAC ACT ATC CAA CAA TTA ATG ATG ATT TTA AAT TCA GCA AGT GAT CAA      1323
Asn Thr Ile Gln Gln Leu Met Met Ile Leu Asn Ser Ala Ser Asp Gln
380                 385                 390                 395

CCT TCA GAA AAT CTG ATT TCC TAT TTT AAC AAC TGC ACA GTG AAT CCA      1371
Pro Ser Glu Asn Leu Ile Ser Tyr Phe Asn Asn Cys Thr Val Asn Pro
                400                 405                 410

AAA GAA AGT ATA CTG AAA AGA GTG AAG GAT ATA GGA TAC ATC TTT AAA      1419
Lys Glu Ser Ile Leu Lys Arg Val Lys Asp Ile Gly Tyr Ile Phe Lys
            415                 420                 425

GAG AAA TTT GCT AAA GCT GTG GGA CAG GGT TGT GTC GAA ATT GGA TCA      1467
Glu Lys Phe Ala Lys Ala Val Gly Gln Gly Cys Val Glu Ile Gly Ser
        430                 435                 440

CAG CGA TAC AAA CTT GGA GTT CGC TTG TAT TAC CGA GTA ATG GAA TCC      1515
Gln Arg Tyr Lys Leu Gly Val Arg Leu Tyr Tyr Arg Val Met Glu Ser
    445                 450                 455

 ATG CTT AAA TCA GAA GAA GAA CGA TTA TCC ATT CAA AAT TTT AGC AAA     1563
Met Leu Lys Ser Glu Glu Glu Arg Leu Ser Ile Gln Asn Phe Ser Lys
460                 465                 470                 475

CTT CTG AAT GAC AAC ATT TTT CAT ATG TCT TTA TTG GCG TGC GCT CTT      1611
Leu Leu Asn Asp Asn Ile Phe His Met Ser Leu Leu Ala Cys Ala Leu
                480                 485                 490

GAG GTT GTA ATG GCC ACA TAT AGC AGA AGT ACA TCT CAG AAT CTT GAT      1659
Glu Val Val Met Ala Thr Tyr Ser Arg Ser Thr Ser Gln Asn Leu Asp
            495                 500                 505

TCT GGA ACA GAT TTG TCT TTC CCA TGG ATT CTG AAT GTG CTT AAT TTA      1707
Ser Gly Thr Asp Leu Ser Phe Pro Trp Ile Leu Asn Val Leu Asn Leu
        510                 515                 520

AAA GCC TTT GAT TTT TAC AAA GTG ATC GAA AGT TTT ATC AAA GCA GAA      1755
Lys Ala Phe Asp Phe Tyr Lys Val Ile Glu Ser Phe Ile Lys Ala Glu
    525                 530                 535
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GGC AAC TTG ACA AGA GAA ATG ATA AAA CAT TTA GAA CGA TGT GAA CAT      1803
Gly Asn Leu Thr Arg Glu Met Ile Lys His Leu Glu Arg Cys Glu His
540                 545                 550                 555

CGA ATC ATG GAA TCC CTT GCA TGG CTC TCA GAT TCA CCT TTA TTT GAT      1851
Arg Ile Met Glu Ser Leu Ala Trp Leu Ser Asp Ser Pro Leu Phe Asp
                560                 565                 570

CTT ATT AAA CAA TCA AAG GAC CGA GAA GGA CCA ACT GAT CAC CTT GAA      1899
Leu Ile Lys Gln Ser Lys Asp Arg Glu Gly Pro Thr Asp His Leu Glu
            575                 580                 585

TCT GCT TGT CCT CTT AAT CTT CCT CTC CAG AAT AAT CAC ACT GCA GCA      1947
Ser Ala Cys Pro Leu Asn Leu Pro Leu Gln Asn Asn His Thr Ala Ala
        590                 595                 600

GAT ATG TAT CTT TCT CCT GTA AGA TCT CCA AAG AAA AAA GGT TCA ACT      1995
Asp Met Tyr Leu Ser Pro Val Arg Ser Pro Lys Lys Lys Gly Ser Thr
    605                 610                 615

ACG CGT GTA AAT TCT ACT GCA AAT GCA GAG ACA CAA GCA ACC TCA GCC      2043
Thr Arg Val Asn Ser Thr Ala Asn Ala Glu Thr Gln Ala Thr Ser Ala
620                 625                 630                 635

TTC CAG ACC CAG AAG CCA TTG AAA TCT ACC TCT CTT TCA CTG TTT TAT      2091
Phe Gln Thr Gln Lys Pro Leu Lys Ser Thr Ser Leu Ser Leu Phe Tyr
                640                 645                 650

AAA AAA GTG TAT CGG CTA GCC TAT CTC CGG CTA AAT ACA CTT TGT GAA      2139
Lys Lys Val Tyr Arg Leu Ala Tyr Leu Arg Leu Asn Thr Leu Cys Glu
            655                 660                 665

CGC CTT CTG TCT GAG CAC CCA GAA TTA GAA CAT ATC ATC TGG ACC CTT      2187
Arg Leu Leu Ser Glu His Pro Glu Leu Glu His Ile Ile Trp Thr Leu
        670                 675                 680

TTC CAG CAC ACC CTG CAG AAT GAG TAT GAA CTC ATG AGA GAC AGG CAT      2235
Phe Gln His Thr Leu Gln Asn Glu Tyr Glu Leu Met Arg Asp Arg His
    685                 690                 695

TTG GAC CAA ATT ATG ATG TGT TCC ATG TAT GGC ATA TGC AAA GTG AAG      2283
Leu Asp Gln Ile Met Met Cys Ser Met Tyr Gly Ile Cys Lys Val Lys
700                 705                 710                 715

AAT ATA GAC CTT AAA TTC AAA ATC ATT GTA ACA GCA TAC AAG GAT CTT      2331
Asn Ile Asp Leu Lys Phe Lys Ile Ile Val Thr Ala Tyr Lys Asp Leu
                720                 725                 730

CCT CAT GCT GTT CAG GAG ACA TTC AAA CGT GTT TTG ATC AAA GAA GAG      2379
Pro His Ala Val Gln Glu Thr Phe Lys Arg Val Leu Ile Lys Glu Glu
            735                 740                 745
GAG TAT GAT TCT ATT ATA GTA TTC TAT AAC TCG GTC TTC ATG CAG AGA      2427
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Glu Tyr Asp Ser Ile Ile Val Phe Tyr Asn Ser Val Phe Met Gln Arg
        750                 755                 760

CTG AAA ACA AAT ATT TTG CAG TAT GCT TCC ACC AGG CCC CCT ACC TTG      2475
Leu Lys Thr Asn Ile Leu Gln Tyr Ala Ser Thr Arg Pro Pro Thr Leu
    765                 770                 775

TCA CCA ATA CCT CAC ATT CCT CGA AGC CCT TAC AAG TTT CCT AGT TCA      2523
Ser Pro Ile Pro His Ile Pro Arg Ser Pro Tyr Lys Phe Pro Ser Ser
780                 785                 790                 795

CCC TTA CGG ATT CCT GGA GGG AAC ATC TAT ATT TCA CCC CTG AAG AGT      2571
Pro Leu Arg Ile Pro Gly Gly Asn Ile Tyr Ile Ser Pro Leu Lys Ser
                800                 805                 810

CCA TAT AAA ATT TCA GAA GGT CTG CCA ACA CCA ACA AAA ATG ACT CCA      2619
Pro Tyr Lys Ile Ser Glu Gly Leu Pro Thr Pro Thr Lys Met Thr Pro
            815                 820                 825

AGA TCA AGA ATC TTA GTA TCA ATT GGT GAA TCA TTC GGG ACT TCT GAG      2667
Arg Ser Arg Ile Leu Val Ser Ile Gly Glu Ser Phe Gly Thr Ser Glu
        830                 835                 840

AAG TTC CAG AAA ATA AAT CAG ATG GTA TGT AAC AGC GAC CGT GTG CTC      2715
Lys Phe Gln Lys Ile Asn Gln Met Val Cys Asn Ser Asp Arg Val Leu
    845                 850                 855

AAA AGA AGT GCT GAA GGA AGC AAC CCT CCT AAA CCA CTG AAA AAA CTA      2763
Lys Arg Ser Ala Glu Gly Ser Asn Pro Pro Lys Pro Leu Lys Lys Leu
860                 865                 870                 875

CGC TTT GAT ATT GAA GGA TCA GAT GAA GCA GAT GGA AGT AAA CAT CTC      2811
Arg Phe Asp Ile Glu Gly Ser Asp Glu Ala Asp Gly Ser Lys His Leu
                880                 885                 890

CCA GGA GAG TCC AAA TTT CAG CAG AAA CTG GCA GAA ATG ACT TCT ACT      2859
Pro Gly Glu Ser Lys Phe Gln Gln Lys Leu Ala Glu Met Thr Ser Thr
            895                 900                 905

CGA ACA CGA ATG CAA AAG CAG AAA ATG AAT GAT AGC ATG GAT ACC TCA      2907
Arg Thr Arg Met Gln Lys Gln Lys Met Asn Asp Ser Met Asp Thr Ser
        910                 915                 920

AAC AAG GAA GAG AAA TGAGGATCTC AGGACCTTGG TGGACACTGT GTACACCTCT      2962
Asn Lys Glu Glu Lys
    925

GGATTCATTG TCTCTCACAG ATGTGACTGT AT                                  2994
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TABLE 4

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TTCCGGTTTT TCTCAGGGGA CGTTGAAATT ATTTTTGTAA CGGGAGTCGG GAGAGGACGG        60

GGCGTGCCCC GCGTCCGCGC GCGTCGTCCT CCCCGGCGCT CCTCCACAGC TCGCTGGCTC       120

CCGCCGCGGA AAGGCGTC ATG CCG CCC AAA ACC CCC CGA AAA ACG GCC GCC          171
                   Met Pro Pro Lys Thr Pro Arg Lys Thr Ala Ala
                     1               5                  10

ACC GCC GCC GCT GCC GCC GCG GAA CCC CCG GCA CCG CCG CCG CCG CCC          219
Thr Ala Ala Ala Ala Ala Ala Glu Pro Pro Ala Pro Pro Pro Pro Pro
            15                  20                  25

CCT CCG TAG GAG GAC CCA GAG CAG GAC AGC GGC CCG GAG GAC CTG CCT         267
Pro Pro Glu Glu Asp Pro Glu Gln Asp Ser Gly Pro Glu Asp Leu Pro
        30                  35                  40

CTC GTC AGG CTT GAG TTT GAA GAA ACA GAA GAA CCT GAT TTT ACT GCA         315
Leu Val Arg Leu Glu Phe Glu Glu Thr Glu Glu Pro Asp Phe Thr Ala
    45                  50                  55

TTA TGT CAG AAA TTA AAG ATA CCA GAT CAT GTC AGA GAG AGA GCT TGG         363
Leu Cys Gln Lys Leu Lys Ile Pro Asp His Val Arg Glu Arg Ala Trp
60                  65                  70                  75

TTA ACT TGG GAG AAA GTT TCA TCT GTG GAT GGA GTA TTG GGA GGT TAT         411
Leu Thr Trp Glu Lys Val Ser Ser Val Asp Gly Val Leu Gly Gly Tyr
                80                  85                  90

ATT CAA AAG AAA AAG GAA CTG TGG GGA ATC TGT ATC TTT ATT GCA GCA         459
Ile Gln Lys Lys Lys Glu Leu Trp Gly Ile Cys Ile Phe Ile Ala Ala
            95                  100                 105

GTT GAC CTA GAT GAG ATG TCG TTC ACT TTT ACT GAG CTA CAG AAA AAC         507
Val Asp Leu Asp Glu Met Ser Phe Thr Phe Thr Glu Leu Gln Lys Asn
        110                 115                 120

ATA GAA ATC AGT GTC CAT AAA TTC TTT AAC TTA CTA AAA GAA ATT GAT         555
Ile Glu Ile Ser Val His Lys Phe Phe Asn Leu Leu Lys Glu Ile Asp
    125                 130                 135

ACC AGT ACC AAA GTT GAT AAT GCT ATG TCA AGA CTG TTG AAG AAG TAT         603
Thr Ser Thr Lys Val Asp Asn Ala Met Ser Arg Leu Leu Lys Lys Tyr
140                 145                 150                 155

GAT GTA TTG TTT GCA CTC TTC AGC AAA TTG GAA AGG ACA TGT GAA CTT         651
Asp Val Leu Phe Ala Leu Phe Ser Lys Leu Glu Arg Thr Cys Glu Leu
                160                 165                 170
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ATA TAT TTG ACA CAA CCC AGC AGT TCG ATA TCT ACT GAA ATA AAT TCT 699
Ile Tyr Leu Thr Gln Pro Ser Ser Ser Ile Ser Thr Glu Ile Asn Ser
175 180 185

GCA TTG GTC CTA AAA GTT TCT TGG ATC ACA TTT TTA TTA GCT AAA GGG 747
Ala Leu Val Leu Lys Val Ser Trp Ile Thr Phe Leu Leu Ala Lys Gly
190 195 200

GAA GTA TTA CAA ATG GAA GAT GAT CTG GTG ATT TCA TTT CAG TTA ATG 795
Glu Val Leu Gln Met Glu Asp Asp Leu Val Ile Ser Phe Gln Leu Met
205 210 215

CTA TGT GTC CTT GAC TAT TTT ATT AAA CTC TCA CCT CCC ATG TTG CTC 843
Leu Cys Val Leu Asp Tyr Phe Ile Lys Leu Ser Pro Pro Met Leu Leu
220 225 230 235

AAA GAA CCA TAT AAA ACA GCT GTT ATA CCC ATT AAT GGT TCA CCT CGA 891
Lys Glu Pro Tyr Lys Thr Ala Val Ile Pro Ile Asn Gly Ser Pro Arg
240 245 250

ACA CCC AGG CGA GGT CAG AAC AGG AGT GCA CGG ATA GCA AAA CAA CTA 939
Thr Pro Arg Arg Gly Gln Asn Arg Ser Ala Arg Ile Ala Lys Gln Leu
255 260 265

GAA AAT GAT ACA AGA ATT ATT GAA GTT CTC TGT AAA GAA CAT GAA TGT 987
Glu Asn Asp Thr Arg Ile Ile Glu Val Leu Cys Lys Glu His Glu Cys
270 275 280

AAT ATA GAT GAG GTG AAA AAT GTT TAT TTC AAA AAT TTT ATA CCT TTT 1035
Asn Ile Asp Glu Val Lys Asn Val Tyr Phe Lys Asn Phe Ile Pro Phe
285 290 295

ATG AAT TCT CTT GGA CTT GTA ACA TCT AAT GGA CTT CCA GAG GTT GAA 1083
Met Asn Ser Leu Gly Leu Val Thr Ser Asn Gly Leu Pro Glu Val Glu
300 305 310 315

AAT CTT TCT AAA CGA TAC GAA GAA ATT TAT CTT AAA AAT AAA GAT CTA 1131
Asn Leu Ser Lys Arg Tyr Glu Glu Ile Tyr Leu Lys Asn Lys Asp Leu
320 325 330

GAT GCA AGA TTA TTT TTG GAT CAT GAT AAA ACT CTT CAG ACT GAT TCT 1179
Asp Ala Arg Leu Phe Leu Asp His Asp Lys Thr Leu Gln Thr Asp Ser
335 340 345

ATA GAC AGT TTT GAA ACA CAG AGA ACA CCA CGA AAA AGT AAC CTT GAT 1227
Ile Asp Ser Phe Glu Thr Gln Arg Thr Pro Arg Lys Ser Asn Leu Asp
350 355 360

GAA GAG GTG AAT GTA ATT CCT CCA CAC ACT CCA GTT AGG ACT GTT ATG 1275
Glu Glu Val Asn Val Ile Pro Pro His Thr Pro Val Arg Thr Val Met
365 370 375

AAC ACT ATC CAA CAA TTA ATG ATG ATT TTA AAT TCA GCA AGT GAT CAA 1323
Asn Thr Ile Gln Gln Leu Met Met Ile Leu Asn Ser Ala Ser Asp Gln
380 385 390 395

CCT TCA GAA AAT CTG ATT TCC TAT TTT AAC AAC TGC ACA GTG AAT CCA 1371
Pro Ser Glu Asn Leu Ile Ser Tyr Phe Asn Asn Cys Thr Val Asn Pro
400 405 410

AAA GAA AGT ATA CTG AAA AGA GTG AAG GAT ATA GGA TAC ATC TTT AAA 1419
Lys Glu Ser Ile Leu Lys Arg Val Lys Asp Ile Gly Tyr Ile Phe Lys
415 420 425

GAG AAA TTT GCT AAA GCT GTG GGA CAG GGT TGT GTC GAA ATT GGA TCA 1467
Glu Lys Phe Ala Lys Ala Val Gly Gln Gly Cys Val Glu Ile Gly Ser
430 435 440

CAG CGA TAC AAA CTT GGA GTT CGC TTG TAT TAC CGA GTA ATG GAA TCC 1515
Gln Arg Tyr Lys Leu Gly Val Arg Leu Tyr Tyr Arg Val Met Glu Ser
445 450 455

ATG CTT AAA TCA GAA GAA GAA CGA TTA TCC ATT CAA AAT TTT AGC AAA 1563
Met Leu Lys Ser Glu Glu Glu Arg Leu Ser Ile Gln Asn Phe Ser Lys
460 465 470 475

CTT CTG AAT GAC AAC ATT TTT CAT ATG TCT TTA TTG GCG TGC GCT CTT 1611
Leu Leu Asn Asp Asn Ile Phe His Met Ser Leu Leu Ala Cys Ala Leu
480 485 490

GAG GTT GTA ATG GCC ACA TAT AGC AGA AGT ACA TCT CAG AAT CTT GAT 1659
Glu Val Val Met Ala Thr Tyr Ser Arg Ser Thr Ser Gln Asn Leu Asp
495 500 505

TCT GGA ACA GAT TTG TCT TTC CCA TGG ATT CTG AAT GTG CTT AAT TTA 1707
Ser Gly Thr Asp Leu Ser Phe Pro Trp Ile Leu Asn Val Leu Asn Leu
510 515 520

AAA GCC TTT GAT TTT TAC AAA GTG ATC GAA AGT TTT ATC AAA GCA GAA 1755
Lys Ala Phe Asp Phe Tyr Lys Val Ile Glu Ser Phe Ile Lys Ala Glu
525 530 535

GGC AAC TTG ACA AGA GAA ATG ATA AAA CAT TTA GAA CGA TGT GAA CAT 1803
Gly Asn Leu Thr Arg Glu Met Ile Lys His Leu Glu Arg Cys Glu His
540 545 550 555

CGA ATC ATG GAA TCC CTT GCA TGG CTC TCA GAT TCA CCT TTA TTT GAT 1851
Arg Ile Met Glu Ser Leu Ala Trp Leu Ser Asp Ser Pro Leu Phe Asp
560 565 570

CTT ATT AAA CAA TCA AAG GAC CGA GAA GGA CCA ACT GAT CAC CTT GAA 1899
Leu Ile Lys Gln Ser Lys Asp Arg Glu Gly Pro Thr Asp His Leu Glu
575 580 585

~~TCT GCT TGT CCT CTT AAT CTT CCT CTC CAG AAT AAT CAC ACT GCA GCA 1947~~
~~Ser Ala Cys Pro Leu Asn Leu Pro Leu Gln Asn Asn His Thr Ala Ala~~
~~590 595 600~~

~~GAT ATG TAT CTT TCT CCT GTA AGA TCT CCA AAG AAA AAA GGT TCA ACT 1995~~
~~Asp Met Tyr Leu Ser Pro Val Arg Ser Pro Lys Lys Lys Gly Ser Thr~~
~~605 610 615~~

~~ACG CGT GTA AAT TCT ACT GCA AAT GCA GAG ACA CAA GCA ACC TCA GCC 2043~~
~~Thr Arg Val Asn Ser Thr Ala Asn Ala Glu Thr Gln Ala Thr Ser Ala~~
~~620 625 630 635~~

~~TTC CAG ACC CAG AAG CCA TTG AAA TCT ACC TCT CTT TCA CTG TTT TAT 2091~~
~~Phe Gln Thr Gln Lys Pro Leu Lys Ser Thr Ser Leu Ser Leu Phe Tyr~~
~~640 645 650~~

~~AAA AAA GTG TAT CGG CTA GCC TAT CTC CGG CTA AAT ACA CTT TGT GAA 2139~~
~~Lys Lys Val Tyr Arg Leu Ala Tyr Leu Arg Leu Asn Thr Leu Cys Glu~~
~~655 660 665~~

~~CGC CTT CTG TCT GAG CAC CCA GAA TTA GAA CAT ATC ATC TGG ACC CTT 2187~~
~~Arg Leu Leu Ser Glu His Pro Glu Leu Glu His Ile Ile Trp Thr Leu~~
~~670 675 680~~

~~TTC CAG CAC ACC CTG CAG AAT GAG TAT GAA CTC ATG AGA GAC AGG CAT 2235~~
~~Phe Gln His Thr Leu Gln Asn Glu Tyr Glu Leu Met Arg Asp Arg His~~
~~685 690 695~~

~~TTG GAC CAA ATT ATG ATG TGT TCC ATG TAT GGC ATA TGC AAA GTG AAG 2283~~
~~Leu Asp Gln Ile Met Met Cys Ser Met Tyr Gly Ile Cys Lys Val Lys~~
~~700 705 710 715~~

~~AAT ATA GAC CTT AAA TTC AAA ATC ATT GTA ACA GCA TAC AAG GAT CTT 2331~~
~~Asn Ile Asp Leu Lys Phe Lys Ile Ile Val Thr Ala Tyr Lys Asp Leu~~
~~720 725 730~~

~~CCT CAT GCT GTT CAG GAG ACA TTC AAA CGT GTT TTG ATC AAA GAA GAG 2379~~
~~Pro His Ala Val Gln Glu Thr Phe Lys Arg Val Leu Ile Lys Glu Glu~~
~~735 740 745~~

~~GAG TAT GAT TCT ATT ATA GTA TTC TAT AAC TCG GTC TTC ATG CAG AGA 2427~~
~~Glu Tyr Asp Ser Ile Ile Val Phe Tyr Asn Ser Val Phe Met Gln Arg~~
~~750 755 760~~

~~CTG AAA ACA AAT ATT TTG CAG TAT GCT TCC ACC AGG CCC CCT ACC TTG 2475~~
~~Leu Lys Thr Asn Ile Leu Gln Tyr Ala Ser Thr Arg Pro Pro Thr Leu~~
~~765 770 775~~

~~TCA CCA ATA CCT CAC ATT CCT CGA AGC CCT TAC AAG TTT CCT AGT TCA 2523~~
~~Ser Pro Ile Pro His Ile Pro Arg Ser Pro Tyr Lys Phe Pro Ser Ser~~
~~780 785 790 795~~

~~CCC TTA CGG ATT CCT GGA GGG AAC ATC TAT ATT TCA CCC CTG AAG AGT~~ 2571
~~Pro Leu Arg Ile Pro Gly Gly Asn Ile Tyr Ile Ser Pro Leu Lys Ser~~
~~800 805 810~~

~~CCA TAT AAA ATT TCA GAA GGT CTG CCA ACA CCA ACA AAA ATG ACT CCA~~ 2619
~~Pro Tyr Lys Ile Ser Glu Gly Leu Pro Thr Pro Thr Lys Met Thr Pro~~
~~815 820 825~~

~~AGA TCA AGA ATC TTA GTA TCA ATT GGT GAA TCA TTC GGG ACT TCT GAG~~ 2667
~~Arg Ser Arg Ile Leu Val Ser Ile Gly Glu Ser Phe Gly Thr Ser Glu~~
~~830 835 840~~

~~AAG TTC CAG AAA ATA AAT CAG ATG GTA TGT AAC AGC GAC CGT GTG CTC~~ 2715
~~Lys Phe Gln Lys Ile Asn Gln Met Val Cys Asn Ser Asp Arg Val Leu~~
~~845 850 855~~

~~AAA AGA ACT GCT GAA GGA AGC AAC CCT CCT AAA CCA CTG AAA AAA CTA~~ 2763
~~Lys Arg Ser Ala Glu Gly Ser Asn Pro Pro Lys Pro Leu Lys Lys Leu~~
~~860 865 870 875~~

~~CGC TTT GAT ATT GAA GGA TCA GAT GAA GCA GAT GGA AGT AAA CAT CTC~~ 2811
~~Arg Phe Asp Ile Glu Gly Ser Asp Glu Ala Asp Gly Ser Lys His Leu~~
~~880 885 890~~

~~CCA GGA GAG TCC AAA TTT CAG CAG AAA CTG GCA GAA ATG ACT TCT ACT~~ 2859
~~Pro Gly Glu Ser Lys Phe Gln Gln Lys Leu Ala Glu Met Thr Ser Thr~~
~~895 900 905~~

~~CGA ACA CGA ATG CAA AAG CAG AAA ATG AAT GAT AGC ATG GAT ACC TCA~~ 2907
~~Arg Thr Arg Met Gln Lys Gln Lys Met Asn Asp Ser Met Asp Thr Ser~~
~~910 915 920~~

~~AAC AAG GAA GAG AAA TGAGGATCTC AGGACCTTGG TGGACACTGT GTACACCTCT~~ 2962
~~Asn Lys Glu Glu Lys~~
~~925~~

~~GGATTCATTG TCTCTCACAG ATGTGACTGT AT~~ 2994
--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 10, at the end of the application.

In the Claims:

Please amend claims 35, 39 and 40 as follows:

1. (Original) A method of controlling cancer suppression in a mammal having a cancer suppressing gene, comprising the steps of:

making a substantially duplicated genetic material corresponding to the genetic material of said gene, the substantially duplicated material selected from the group consisting of a cloned cancer suppressing gene, a modified or defective cancer suppressing gene, homologues thereof, fragments thereof, and mixtures thereof; and

interchanging said duplicated genetic material and the cancer suppressing gene of the mammal.

2. (Original) A method of claim 1, wherein before said making a substantially duplicated genetic material, determining the chromosomal location of said cancer suppressing gene of the mammal.

3. (Original) A method of claim 1, wherein after said making a substantially duplicated genetic material, detecting the presence or absence of an inactive cancer suppressing gene of a tissue sample of the mammal to determine whether or not the tissue sample cancer suppressing gene is defective or absent.

4. (Original) A method of claim 3, wherein in response to a determination that the tissue sample cancer suppressing gene is either defective or absent, replacing a cancer suppressing gene of the mammal with its clone.

5. (Original) A method of claim 3, wherein the determination of whether or not the tissue sample cancer suppressing gene is defective or absent is accomplished by measuring the amount of protein product of said cancer suppressing gene, of the tissue sample, bound by an antibody specific for said protein.

6. (Original) A method of claim 5, wherein the determination of whether or not the tissue sample cancer suppressing gene is defective or absent is accomplished by:

(a) labeling said tissue sample with radioactive isotope;

(b) lysing the labeled tissue;

(c) reacting the protein product of said cancer suppressing gene with an antibody specific for said protein thereby forming a protein/antibody immunocomplex;

(d) autoradiographing the immunocomplex obtained in step (c); and

(e) determining the presence or absence of the protein product by comparing the autoradiogram of step (d) with the autoradiogram of the standard protein product.

7. (Original) The method of claim 5, wherein the determination of whether or not the tissue sample cancer suppressing gene is defective or absent is accomplished by enzyme immunoassay techniques.

8. (Original) The method of claim 5, wherein the determination of whether or not the tissue sample cancer suppressing gene is defective or absent is accomplished by immunocytochemistry methods.

9. (Original) The method of claim 5, wherein the cancer suppressing gene is the RB gene and the protein product is $ppRB^{110}$.

10. (Original) The method of claim 1, wherein said cancer suppressing gene is replaced with substantially duplicated material selected from the group consisting of said cloned cancer suppressing gene, homologues thereof, fragments thereof, and mixtures thereof, for therapeutic purposes.

11. (Original) The method of claim 1, wherein said cancer suppressing gene is replaced with substantially duplicated material selected from the group consisting of said defective cancer suppressing gene, homologues thereof, fragments thereof, and mixtures thereof, for facilitating the testing of the carcinogenicity of environmental influences.

12. (Original) The method of claim 2, wherein the location of said cancer suppressing gene is determined by chromosome walking.

13. (Original) The method of claim 2, wherein the location of said cancer suppressing gene is determined through organic markers.

14. (Original) A method of claim 2, wherein:

said chromosomal location of said cancer suppressing gene is determined by testing genes of a chromosome for phenotypic expression;

determining one of the genes of said chromosome to be a marker gene; and

using chromosomal walking techniques to locate a cancer suppressing gene.

15. (Original) An animal genetically altered so as to have the allele of at least one cancer suppressing gene selected from the group consisting of a defective allele, a homologue thereof, a fragment thereof, and a mixture thereof.

16. (Original) An animal of claim 15, wherein said defective allele is selected from the group consisting of defective alleles of RB genes, breast cancer suppressing genes, Wilm's tumor suppressing genes, Beckwith-Wiedemann syndrome suppressing genes, bladder transitional cell carcinoma suppressing genes, neuroblastoma suppressing genes, small cell lung carcinoma suppressing genes, renal cell carcinoma suppressing genes, acoustic neuroma suppressing genes, colorectal carcinoma suppressing genes, homolgues thereof, fragments thereof, and mixtures thereof.

17. (Original) An animal of claim 15, wherein said allele contains a DNA fragment having at least one defective nucleotide sequence.

18. (Original) An animal of claim 15, wherein said defective allele contains a DNA fragment having at least one defective RB nucleotide sequence.

19. (Original) The animal of claim 15, wherein said animal is a mouse.

20. (Original) A method for determining the carcinogenicity of suspected environmental influences, using the animal of claim 14, comprising the steps of:

exposing said animal to a suspected environmental influence;

observing the animal for the phenotypic expression of cancer; and

determining carcinogenicity of the suspected environmental influence in response to observing a phenotypic expression of cancer in the animal.

21. (Original) A method of claim 20, wherein said exposing includes exposing to a source of radiation.

22. (Original) A method of claim 20, wherein said exposing includes exposing to tobacco combustion products.

23. (Original) A method of claim 20, wherein said exposing includes exposing to food additives.

24. (Original) A method of claim 20, wherein said exposing includes exposing to artificial substances.

25. (Original) A method of claim 20, wherein said observing includes examining the animal for tumor development.

26. (Original) A method of claim 25, wherein in response to the formation of a tumor in the animal, analyzing the tumor for the presence of cancer cells.

27. (Original) A method of making the animal of claim 15, comprising:

using at least one allele of an animal cancer suppressing gene selected from the group consisting of a defective allele, a homologue thereof, a fragment thereof, and a mixture thereof;

mutating at least one animal cell with said allele to form a mutated cell;

introducing said mutated cell into an animal blastocyst;

permitting growth of the blastocyst for a given period of time sufficient to incorporate said allele into its cells; repressing genetic recombinations within said cells; transferring the blastocyst containing said allele into the uterus of a pseudo pregnant animal for giving birth subsequently to an animal bearing said allele;

breeding said animal to reproduce additional animals; and

selecting the animal of claim 14 from said additional animals by determining the presence therein of the said allele.

28. (Original) A method of claim 27, wherein before introducing said allele, removing said blastocyst from a super ovulated animal, and wherein said blastocyst is comprised of undifferentiated cells.

29. (Original) A method of claim 27, wherein said introducing is performed in vitro.

30. (Original) A pharmaceutical composition wherein the active ingredient is selected from the group consisting of a naturally occurring intact cancer suppressing gene, a cloned intact cancer suppressing gene, fragments thereof, homolgues thereof and mixtures thereof.

31. (Original) A pharmaceutical composition of claim 30, wherein said naturally occurring and cloned cancer suppressing gene is selected from the group consisting of RB genes, breast cancer suppressing genes, Wilm's tumor suppressing genes, Beckwith-Wiedemann syndrome suppressing genes, bladder transitional cell carcinoma suppressing genes, neuroblastoma suppressing genes, small cell lung carcinoma suppressing genes, renal cell carcinoma suppressing genes, acoustic neuroma suppressing genes, colorectal carcinoma suppressing genes, homolgues thereof, fragments thereof, and mixtures thereof.

32. (Original) A pharmaceutical composition of claim 30, wherein the active ingredient is selected from the group consisting of RB cDNA, modified RB cDNA fragment, clones thereof, homolgues thereof and mixtures thereof.

33. (Original) A pharmaceutical composition of claim 31, wherein the active ingredient for each of said gene is selected from the group consisting od cDNA of said gene, fragments of said cDNA, homologues thereof and mixtures thereof.

34. (Original) A pharmaceutical composition of claim 32, wherein the cancer suppressing gene is isolated from human chromosome 13 region 13q14.

35. (Currently amended) A pharmaceutical composition of claim 31, wherein the cancer suppressing gene and its clone each has the ~~following~~ nucleotide sequence comprising SEQ ID NO:1.~~:~~

~~TTCCGGTTTT TCTCAGGGGA CGTTGAAATT ATTTTTGTAA CGGGAGTCGG GAGAGGACGG~~ 60

~~GGCGTGCCCC GCGTGCGCGC GCGTCGTCCT CCCCGGCGCT CCTCCACAGC TCGCTGGCTC~~ 120

~~CCGCCGCGGA AAGGCGTC ATG CCG CCC AAA ACC CCC CGA AAA ACG GCC GCC~~ 171
~~Met Pro Pro Lys Thr Pro Arg Lys Thr Ala Ala~~
~~1 5 10~~

~~ACC GCC GCC GCT GCC GCC GCG GAA CCC CCG GCA CCG CCG CCG CCG CCC~~ 219
~~Thr Ala Ala Ala Ala Ala Ala Glu Pro Pro Ala Pro Pro Pro Pro Pro~~
~~15 20 25~~

~~CCT CCG TAG GAG GAC CCA GAG CAG GAC AGC GGC CCG GAG GAC CTG CCT~~ 267
~~Pro Pro Glu Glu Asp Pro Glu Gln Asp Ser Gly Pro Glu Asp Leu Pro~~
~~30 35 40~~

~~CTC GTC AGG CTT GAG TTT GAA GAA ACA GAA GAA CCT GAT TTT ACT GCA~~ 315
~~Leu Val Arg Leu Glu Phe Glu Glu Thr Glu Glu Pro Asp Phe Thr Ala~~
~~45 50 55~~

~~TTA TGT CAG AAA TTA AAG ATA CCA GAT CAT GTC AGA GAG AGA GCT TGG~~ 363
~~Leu Cys Gln Lys Leu Lys Ile Pro Asp His Val Arg Glu Arg Ala Trp~~
~~60 65 70 75~~

~~TTA ACT TGG GAG AAA GTT TCA TCT GTG GAT GGA GTA TTG GGA GGT TAT~~ 411
~~Leu Thr Trp Glu Lys Val Ser Ser Val Asp Gly Val Leu Gly Gly Tyr~~
~~80 85 90~~

~~ATT CAA AAG AAA AAG GAA CTG TGG GGA ATC TGT ATC TTT ATT GCA GCA~~ 459
~~Ile Gln Lys Lys Lys Glu Leu Trp Gly Ile Cys Ile Phe Ile Ala Ala~~
~~95 100 105~~

~~GTT GAC CTA GAT GAG ATG TCG TTC ACT TTT ACT GAG CTA CAG AAA AAC~~ 507
~~Val Asp Leu Asp Glu Met Ser Phe Thr Phe Thr Glu Leu Gln Lys Asn~~
~~110 115 120~~

~~ATA GAA ATC AGT GTC CAT AAA TTC TTT AAC TTA CTA AAA GAA ATT GAT~~ 555
~~Ile Glu Ile Ser Val His Lys Phe Phe Asn Leu Leu Lys Glu Ile Asp~~
~~125 130 135~~

~~ACC AGT ACC AAA GTT GAT AAT GCT ATG TCA AGA CTG TTG AAG AAG TAT 603~~
~~Thr Ser Thr Lys Val Asp Asn Ala Met Ser Arg Leu Leu Lys Lys Tyr~~
~~140 145 150 155~~

~~GAT GTA TTG TTT GCA CTC TTC AGC AAA TTG GAA AGG ACA TGT GAA CTT 651~~
~~Asp Val Leu Phe Ala Leu Phe Ser Lys Leu Glu Arg Thr Cys Glu Leu~~
~~160 165 170~~

~~ATA TAT TTG ACA CAA CCC AGC AGT TCG ATA TCT ACT GAA ATA AAT TCT 699~~
~~Ile Tyr Leu Thr Gln Pro Ser Ser Ser Ile Ser Thr Glu Ile Asn Ser~~
~~175 180 185~~

~~GCA TTG GTG CTA AAA GTT TCT TGG ATC ACA TTT TTA TTA GCT AAA GGG 747~~
~~Ala Leu Val Leu Lys Val Ser Trp Ile Thr Phe Leu Leu Ala Lys Gly~~
~~190 195 200~~

~~GAA GTA TTA CAA ATG GAA GAT GAT CTG GTG ATT TCA TTT CAG TTA ATG 795~~
~~Glu Val Leu Gln Met Glu Asp Asp Leu Val Ile Ser Phe Gln Leu Met~~
~~205 210 215~~

~~CTA TGT GTC CTT GAC TAT TTT ATT AAA CTC TCA CCT CCC ATG TTG CTC 843~~
~~Leu Cys Val Leu Asp Tyr Phe Ile Lys Leu Ser Pro Pro Met Leu Leu~~
~~220 225 230 235~~

~~AAA GAA CCA TAT AAA ACA GCT GTT ATA CCC ATT AAT GGT TCA CCT CGA 891~~
~~Lys Glu Pro Tyr Lys Thr Ala Val Ile Pro Ile Asn Gly Ser Pro Arg~~
~~240 245 250~~

~~ACA CCC AGG CGA GGT CAG AAC AGG AGT GCA CGG ATA GCA AAA CAA CTA 939~~
~~Thr Pro Arg Arg Gly Gln Asn Arg Ser Ala Arg Ile Ala Lys Gln Leu~~
~~255 260 265~~

~~GAA AAT GAT ACA AGA ATT ATT GAA GTT CTC TGT AAA GAA CAT GAA TGT 987~~
~~Glu Asn Asp Thr Arg Ile Ile Glu Val Leu Cys Lys Glu His Glu Cys~~
~~270 275 280~~

~~AAT ATA GAT GAG GTG AAA AAT GTT TAT TTC AAA AAT TTT ATA CCT TTT 1035~~
~~Asn Ile Asp Glu Val Lys Asn Val Tyr Phe Lys Asn Phe Ile Pro Phe~~
~~285 290 295~~

~~ATG AAT TCT CTT CGA CTT GTA ACA TCT AAT GGA CTT CCA GAG GTT GAA 1083~~
~~Met Asn Ser Leu Gly Leu Val Thr Ser Asn Gly Leu Pro Glu Val Glu~~
~~300 305 310 315~~

~~AAT CTT TCT AAA CGA TAC GAA GAA ATT TAT CTT AAA AAT AAA GAT CTA 1131~~
~~Asn Leu Ser Lys Arg Tyr Glu Glu Ile Tyr Leu Lys Asn Lys Asp Leu~~
~~320 325 330~~

~~GAT GCA AGA TTA TTT TTG GAT CAT GAT AAA ACT CTT CAG ACT GAT TCT 1179~~
~~Asp Ala Arg Leu Phe Leu Asp His Asp Lys Thr Leu Gln Thr Asp Ser~~
~~335 340 345~~

ATA GAC AGT TTT GAA ACA CAG AGA ACA CCA CGA AAA AGT AAC CTT GAT 1227
Ile Asp Ser Phe Glu Thr Gln Arg Thr Pro Arg Lys Ser Asn Leu Asp
350 355 360

GAA GAG GTG AAT GTA ATT CCT CCA CAC ACT CCA GTT AGG ACT GTT ATG 1275
Glu Glu Val Asn Val Ile Pro Pro His Thr Pro Val Arg Thr Val Met
365 370 375

AAC ACT ATC CAA CAA TTA ATG ATG ATT TTA AAT TCA GCA AGT GAT CAA 1323
Asn Thr Ile Gln Gln Leu Met Met Ile Leu Asn Ser Ala Ser Asp Gln
380 385 390 395

CCT TCA GAA AAT CTG ATT TCC TAT TTT AAC AAC TGC ACA GTG AAT CCA 1371
Pro Ser Glu Asn Leu Ile Ser Tyr Phe Asn Asn Cys Thr Val Asn Pro
400 405 410

AAA GAA AGT ATA CTG AAA AGA GTG AAG GAT ATA GGA TAC ATC TTT AAA 1419
Lys Glu Ser Ile Leu Lys Arg Val Lys Asp Ile Gly Tyr Ile Phe Lys
415 420 425

GAG AAA TTT GCT AAA GCT GTG GGA CAG GGT TGT GTC GAA ATT GGA TCA 1467
Glu Lys Phe Ala Lys Ala Val Gly Gln Gly Cys Val Glu Ile Gly Ser
430 435 440

CAG CGA TAC AAA CTT GGA GTT CGC TTG TAT TAC CGA GTA ATG GAA TCC 1515
Gln Arg Tyr Lys Leu Gly Val Arg Leu Tyr Tyr Arg Val Met Glu Ser
445 450 455

ATG CTT AAA TCA GAA GAA GAA CGA TTA TCC ATT CAA AAT TTT AGC AAA 1563
Met Leu Lys Ser Glu Glu Glu Arg Leu Ser Ile Gln Asn Phe Ser Lys
460 465 470 475

CTT CTG AAT GAC AAC ATT TTT CAT ATG TCT TTA TTG GCG TGC GCT CTT 1611
Leu Leu Asn Asp Asn Ile Phe His Met Ser Leu Leu Ala Cys Ala Leu
480 485 490

GAG GTT GTA ATG GCC ACA TAT AGC AGA AGT ACA TCT CAG AAT CTT GAT 1659
Glu Val Val Met Ala Thr Tyr Ser Arg Ser Thr Ser Gln Asn Leu Asp
495 500 505

TCT GGA ACA GAT TTG TCT TTC CCA TGG ATT CTG AAT GTG CTT AAT TTA 1707
Ser Gly Thr Asp Leu Ser Phe Pro Trp Ile Leu Asn Val Leu Asn Leu
510 515 520

AAA GCC TTT GAT TTT TAC AAA GTG ATC GAA AGT TTT ATC AAA GCA GAA 1755
Lys Ala Phe Asp Phe Tyr Lys Val Ile Glu Ser Phe Ile Lys Ala Glu
525 530 535

GGC AAC TTG ACA AGA GAA ATG ATA AAA CAT TTA GAA CGA TGT GAA CAT 1803
Gly Asn Leu Thr Arg Glu Met Ile Lys His Leu Glu Arg Cys Glu His
540 545 550 555

CGA ATC ATG GAA TCC CTT GCA TGG CTC TCA GAT TCA CCT TTA TTT GAT 1851
Arg Ile Met Glu Ser Leu Ala Trp Leu Ser Asp Ser Pro Leu Phe Asp
560 565 570

CTT ATT AAA CAA TCA AAG GAC CGA GAA GGA CCA ACT GAT CAC CTT GAA 1899
Leu Ile Lys Gln Ser Lys Asp Arg Glu Gly Pro Thr Asp His Leu Glu
575 580 585

TCT GCT TGT CCT CTT AAT CTT CCT CTC CAG AAT AAT CAC ACT GCA GCA 1947
Ser Ala Cys Pro Leu Asn Leu Pro Leu Gln Asn Asn His Thr Ala Ala
590 595 600

GAT ATG TAT CTT TCT CCT GTA AGA TCT CCA AAG AAA AAA GGT TCA ACT 1995
Asp Met Tyr Leu Ser Pro Val Arg Ser Pro Lys Lys Lys Gly Ser Thr
605 610 615

ACG CGT GTA AAT TCT ACT GCA AAT GCA GAG ACA CAA GCA ACC TCA GCC 2043
Thr Arg Val Asn Ser Thr Ala Asn Ala Glu Thr Gln Ala Thr Ser Ala
620 625 630 635

TTC CAG ACC CAG AAG CCA TTG AAA TCT ACC TCT CTT TCA CTG TTT TAT 2091
Phe Gln Thr Gln Lys Pro Leu Lys Ser Thr Ser Leu Ser Leu Phe Tyr
640 645 650

AAA AAA GTG TAT CGG CTA GCC TAT CTC CGG CTA AAT ACA CTT TGT GAA 2139
Lys Lys Val Tyr Arg Leu Ala Tyr Leu Arg Leu Asn Thr Leu Cys Glu
655 660 665

CGC CTT CTG TCT GAG CAC CCA GAA TTA GAA CAT ATC ATC TGG ACC CTT 2187
Arg Leu Leu Ser Glu His Pro Glu Leu Glu His Ile Ile Trp Thr Leu
670 675 680

TTC CAG CAC ACC CTG CAG AAT GAG TAT GAA CTC ATG AGA GAC AGG CAT 2235
Phe Gln His Thr Leu Gln Asn Glu Tyr Glu Leu Met Arg Asp Arg His
685 690 695

TTG GAC CAA ATT ATG ATG TGT TCC ATG TAT GGC ATA TGC AAA GTG AAG 2283
Leu Asp Gln Ile Met Met Cys Ser Met Tyr Gly Ile Cys Lys Val Lys
700 705 710 715

AAT ATA GAC CTT AAA TTC AAA ATC ATT GTA ACA GCA TAC AAG GAT CTT 2331
Asn Ile Asp Leu Lys Phe Lys Ile Ile Val Thr Ala Tyr Lys Asp Leu
720 725 730

CCT CAT GCT GTT CAG GAG ACA TTC AAA CGT GTT TTG ATC AAA GAA GAG 2379
Pro His Ala Val Gln Glu Thr Phe Lys Arg Val Leu Ile Lys Glu Glu
735 740 745

GAG TAT GAT TCT ATT ATA GTA TTC TAT AAC TCG GTC TTC ATG CAG AGA 2427
Glu Tyr Asp Ser Ile Ile Val Phe Tyr Asn Ser Val Phe Met Gln Arg
750 755 760

~~CTG AAA ACA AAT ATT TTG CAG TAT GCT TCC ACC AGG CCC CCT ACC TTG 2475~~
~~Leu Lys Thr Asn Ile Leu Gln Tyr Ala Ser Thr Arg Pro Pro Thr Leu~~
~~765 770 775~~

~~TCA CCA ATA CCT CAC ATT CCT CGA AGC CCT TAC AAG TTT CCT AGT TCA 2523~~
~~Ser Pro Ile Pro His Ile Pro Arg Ser Pro Tyr Lys Phe Pro Ser Ser~~
~~780 785 790 795~~

~~CCC TTA CGG ATT CCT GGA GGG AAC ATC TAT ATT TCA CCC CTG AAG AGT 2571~~
~~Pro Leu Arg Ile Pro Gly Gly Asn Ile Tyr Ile Ser Pro Leu Lys Ser~~
~~800 805 810~~

~~CCA TAT AAA ATT TCA GAA GGT CTG CCA ACA CCA ACA AAA ATG ACT CCA 2619~~
~~Pro Tyr Lys Ile Ser Glu Gly Leu Pro Thr Pro Thr Lys Met Thr Pro~~
~~815 820 825~~

~~AGA TCA AGA ATC TTA GTA TCA ATT GGT GAA TCA TTC GGG ACT TCT GAG 2667~~
~~Arg Ser Arg Ile Leu Val Ser Ile Gly Glu Ser Phe Gly Thr Ser Glu~~
~~830 835 840~~

~~AAG TTC CAG AAA ATA AAT CAG ATG GTA TGT AAC AGC GAC CGT GTG CTC 2715~~
~~Lys Phe Gln Lys Ile Asn Gln Met Val Cys Asn Ser Asp Arg Val Leu~~
~~845 850 855~~

~~AAA AGA AGT GCT GAA GGA AGC AAC CCT CCT AAA CCA CTG AAA AAA CTA 2763~~
~~Lys Arg Ser Ala Glu Gly Ser Asn Pro Pro Lys Pro Leu Lys Lys Leu~~
~~860 865 870 875~~

~~CGC TTT GAT ATT GAA GGA TCA GAT GAA GCA GAT GGA AGT AAA CAT CTC 2811~~
~~Arg Phe Asp Ile Glu Gly Ser Asp Glu Ala Asp Gly Ser Lys His Leu~~
~~880 885 890~~

~~CCA GGA GAG TCC AAA TTT CAG CAG AAA CTG GCA GAA ATG ACT TCT ACT 2859~~
~~Pro Gly Glu Ser Lys Phe Gln Gln Lys Leu Ala Glu Met Thr Ser Thr~~
~~895 900 905~~

~~CGA ACA CGA ATG CAA AAG CAG AAA ATG AAT GAT AGC ATG GAT ACC TCA 2907~~
~~Arg Thr Arg Met Gln Lys Gln Lys Met Asn Asp Ser Met Asp Thr Ser~~
~~910 915 920~~

~~AAC AAG GAA GAG AAA TGAGGATCTC AGGACCTTGG TGGACACTGT GTACACCTCT 2962~~
~~Asn Lys Glu Glu Lys~~
~~925~~

~~GGATTCATTG TCTCTCACAG ATGTGACTGT AT 2994~~

36. (Original) A pharmaceutical composition of claim 32, wherein said RB cDNA fragment is selected from the group consisting of RB-1, RB-2, RB-5, $_{y}$79R8 and mixtures thereof.

37. (Original) A pharmaceutical composition of claim 32, wherein a resulting mRNA transcript of said RB cDNA fragment has 4.6 kb.

38. (Original) A pharmaceutical composition of claim 37, wherein the cloned genomic DNA has at least 27 exons.

39. (Currently amended) A pharmaceutical composition of claim 30, wherein the cloned RB cDNA transcribes into mRNA which translates in protein having an amino acid sequence comprising SEQ ID NO:2.

~~MPPKTPRKTAATAAAAAAAEPPAPPPPPPPPEEDPE (34)~~
~~QDSGPEDLPLVRLEFEETEEPDFTALCQKLKIPDHVRERA (74)~~
~~WLTWEKVSSVDGVLGGYIQKKKELWGICIFIAAVDLDEMS (114)~~
~~FTFTELQKNIEISVHKFFNLLKEIDTSTKVDNAMSRLLKK (154)~~
~~YDVLFALFSKLERTCELIYLTQPSSSISTEINSALVLKVS (194)~~
~~WITFLLAKGEVLQMEDDLVISFQLNLCVLDYFIKLSPPML (234)~~
~~LKEPYKTAVIPINGSPRTPRRGQMRSARIAKQLENDTRII (274)~~
~~EVLCKEHECNIDEVKNVYFKNFIPFMNSLGLVTSNGLPEV (314)~~
~~ENLSKRYEEIYLKNKDLDARLFLDHDKTLQTDSIDSFETQ (354)~~
~~RTPRKSNLDEEVNVIPPHTPVRTVMNTIQQLMMILNSASD (394)~~
~~QPSENLISYFNNCTVNPKESILKRVKDICYIFKEKFAKAV (434)~~
~~GQGCVEIGSQRYKLGVRLYYRVMESMLKSEEERLSIQNFS (474)~~
~~KLLNDNIFHMSLLACALEVVMATYSRSTSQNLDSGTDLSF (514)~~
~~PWILNVLNLKAFDFYKVIESFIKAEGNLTREMIKHLERCE (554)~~
~~HRIMESLAWLSDSPLFDLIKQSKDREGPTDHLESACPLNL (594)~~
~~PLQNNHTAADMYLSPVRSPKKKGSTTRVNSTANAETQATS (634)~~
~~AFQTQKPLKSTSLSLFYKKVYRLAYLRLNTLCERLLSEHP (674)~~
~~ELEHIIWTLFQHTLQNEYELMRDRHLDQIMMCSMYGICKV (714)~~
~~KNIDLKFKIIVTAYKDLPHAVQETFKRVLIKEEEYDSIIV (754)~~
~~FYNSVFMQRLKTNILQYASTRPPTLSPIPHIPRSPYKFPS (794)~~
~~SPLRIPGGNIYISPLKSPYKISEGLPTPTKMTPRSRILVS (834)~~
~~IGESFGTSEKFQKINQMVCNSDRVLKRSAEGSNPPKPLKK (874)~~
~~LRFDIEGSDEADGSKHLPGESKFQQKLAEMTSTRTRMQKQ (914)~~
~~KMNDSMDTSNKEEK (928)~~

~~single letter abbreviations for the amino acid residues are: A, Ala; C, Cys; D, Asp; E, Gly; F, Phe; G, Gly; H, His;~~

~~I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln; R, Arg; S, Ser; T, Thr; V, Val; W, Trp; and Y, Tyr.~~

40. (Currently amended) A DNA nucleotide sequence comprising SEQ ID NO:1.~~:~~

~~TTCCGGTTTT TCTCAGGGGA CGTTGAAATT ATTTTTGTAA CGCGAGTCGG GAGAGGACGG 60~~

~~GGCGTGCCCC GCGTGCGCGC GCGTCGTCCT CCCCGGCGCT CCTCCACAGC TCGCTGGCTC 120~~

~~CCGCCGCCGA AAGGCGTC ATG CCG CCC AAA ACC CCC CGA AAA ACG GCC GCC 171~~
~~Met Pro Pro Lys Thr Pro Arg Lys Thr Ala Ala~~
~~1 5 10~~

~~ACC GCC GCC GCT GCC GCC GCG GAA CCC CCG GCA CCG CCG CCG CCG CCC 219~~
~~Thr Ala Ala Ala Ala Ala Ala Glu Pro Pro Ala Pro Pro Pro Pro Pro~~
~~15 20 25~~

~~CCT CCG TAC GAG GAC CCA GAG CAG GAC AGC GGC CCG GAG GAC CTG CCT 267~~
~~Pro Pro Glu Glu Asp Pro Glu Gln Asp Ser Gly Pro Glu Asp Leu Pro~~
~~30 35 40~~

~~CTC GTC AGG CTT GAG TTT GAA GAA ACA GAA GAA CCT GAT TTT ACT GCA 315~~
~~Leu Val Arg Leu Glu Phe Glu Glu Thr Glu Glu Pro Asp Phe Thr Ala~~
~~45 50 55~~

~~TTA TGT CAC AAA TTA AAG ATA CCA GAT CAT GTC AGA GAG AGA GCT TGG 363~~
~~Leu Cys Gln Lys Leu Lys Ile Pro Asp His Val Arg Glu Arg Ala Trp~~
~~60 65 70 75~~

~~TTA ACT TGG GAG AAA GTT TCA TCT GTG GAT GGA GTA TTG GGA GGT TAT 411~~
~~Leu Thr Trp Glu Lys Val Ser Ser Val Asp Gly Val Leu Gly Gly Tyr~~
~~80 85 90~~

~~ATT CAA AAG AAA AAG GAA CTG TGG GGA ATC TGT ATC TTT ATT GCA GCA 459~~
~~Ile Gln Lys Lys Lys Glu Leu Trp Gly Ile Cys Ile Phe Ile Ala Ala~~
~~95 100 105~~

~~GTT GAC CTA GAT GAG ATG TCG TTC ACT TTT ACT GAG CTA CAG AAA AAC 507~~
~~Val Asp Leu Asp Glu Met Ser Phe Thr Phe Thr Glu Leu Gln Lys Asn~~
~~110 115 120~~

~~ATA GAA ATC AGT GTC CAT AAA TTC TTT AAC TTA CTA AAA GAA ATT GAT 555~~
~~Ile Glu Ile Ser Val His Lys Phe Phe Asn Leu Leu Lys Glu Ile Asp~~
~~125 130 135~~

~~ACC AGT ACC AAA GTT GAT AAT GCT ATG TCA AGA CTG TTG AAG AAG TAT~~ ~~603~~
~~Thr Ser Thr Lys Val Asp Asn Ala Met Ser Arg Leu Leu Lys Lys Tyr~~
~~140 145 150 155~~

~~GAT GTA TTG TTT GCA CTC TTC AGC AAA TTG GAA AGG ACA TGT GAA CTT~~ ~~651~~
~~Asp Val Leu Phe Ala Leu Phe Ser Lys Leu Glu Arg Thr Cys Glu Leu~~
~~160 165 170~~

~~ATA TAT TTG ACA CAA CCC AGC AGT TCG ATA TCT ACT GAA ATA AAT TCT~~ ~~699~~
~~Ile Tyr Leu Thr Gln Pro Ser Ser Ser Ile Ser Thr Glu Ile Asn Ser~~
~~175 180 185~~

~~GCA TTG GTG CTA AAA GTT TCT TGG ATC ACA TTT TTA TTA GCT AAA GGG~~ ~~747~~
~~Ala Leu Val Leu Lys Val Ser Trp Ile Thr Phe Leu Leu Ala Lys Gly~~
~~190 195 200~~

~~GAA GTA TTA CAA ATG GAA GAT GAT CTG GTG ATT TCA TTT CAG TTA ATG~~ ~~795~~
~~Glu Val Leu Gln Met Glu Asp Asp Leu Val Ile Ser Phe Gln Leu Met~~
~~205 210 215~~

~~CTA TGT GTC CTT GAC TAT TTT ATT AAA CTC TCA CCT CCC ATG TTG CTC~~ ~~843~~
~~Leu Cys Val Leu Asp Tyr Phe Ile Lys Leu Ser Pro Pro Met Leu Leu~~
~~220 225 230 235~~

~~AAA GAA CCA TAT AAA ACA GCT GTT ATA CCC ATT AAT CGT TCA CCT CGA~~ ~~891~~
~~Lys Glu Pro Tyr Lys Thr Ala Val Ile Pro Ile Asn Gly Ser Pro Arg~~
~~240 245 250~~

~~ACA CCC ACG CGA CGT CAC AAC ACG AGT GCA CGG ATA GCA AAA CAA CTA~~ ~~939~~
~~Thr Pro Arg Arg Gly Gln Asn Arg Ser Ala Arg Ile Ala Lys Gln Leu~~
~~255 260 265~~

~~GAA AAT GAT ACA AGA ATT ATT GAA GTT CTC TGT AAA GAA CAT GAA TGT~~ ~~987~~
~~Glu Asn Asp Thr Arg Ile Ile Glu Val Leu Cys Lys Glu His Glu Cys~~
~~270 275 280~~

~~AAT ATA GAT GAG GTG AAA AAT GTT TAT TTC AAA AAT TTT ATA CCT TTT~~ ~~1035~~
~~Asn Ile Asp Glu Val Lys Asn Val Tyr Phe Lys Asn Phe Ile Pro Phe~~
~~285 290 295~~

~~ATG AAT TCT CTT GGA CTT GTA ACA TCT AAT GGA CTT CCA GAG GTT GAA~~ ~~1083~~
~~Met Asn Ser Leu Gly Leu Val Thr Ser Asn Gly Leu Pro Glu Val Glu~~
~~300 305 310 315~~

~~AAT CTT TCT AAA CGA TAC GAA GAA ATT TAT CTT AAA AAT AAA GAT CTA~~ ~~1131~~
~~Asn Leu Ser Lys Arg Tyr Glu Glu Ile Tyr Leu Lys Asn Lys Asp Leu~~
~~320 325 330~~

~~GAT GCA AGA TTA TTT TTG GAT CAT GAT AAA ACT CTT CAG ACT GAT TCT~~ ~~1179~~
~~Asp Ala Arg Leu Phe Leu Asp His Asp Lys Thr Leu Gln Thr Asp Ser~~
~~335 340 345~~

ATA GAC AGT TTT GAA ACA CAG AGA ACA CCA CGA AAA AGT AAC CTT GAT 1227
Ile Asp Ser Phe Glu Thr Gln Arg Thr Pro Arg Lys Ser Asn Leu Asp
350 355 360

GAA GAG GTG AAT GTA ATT CCT CCA CAC ACT CCA GTT AGG ACT GTT ATG 1275
Glu Glu Val Asn Val Ile Pro Pro His Thr Pro Val Arg Thr Val Met
365 370 375

AAC ACT ATC CAA CAA TTA ATG ATG ATT TTA AAT TCA GCA AGT GAT CAA 1323
Asn Thr Ile Gln Gln Leu Met Met Ile Leu Asn Ser Ala Ser Asp Gln
380 385 390 395

CCT TCA GAA AAT CTG ATT TCC TAT TTT AAC AAC TGC ACA GTG AAT CCA 1371
Pro Ser Glu Asn Leu Ile Ser Tyr Phe Asn Asn Cys Thr Val Asn Pro
400 405 410

AAA GAA AGT ATA CTG AAA AGA GTG AAG GAT ATA GGA TAC ATC TTT AAA 1419
Lys Glu Ser Ile Leu Lys Arg Val Lys Asp Ile Gly Tyr Ile Phe Lys
415 420 425

GAG AAA TTT GCT AAA GCT GTG GGA CAG GGT TGT GTC GAA ATT GGA TCA 1467
Glu Lys Phe Ala Lys Ala Val Gly Gln Gly Cys Val Glu Ile Gly Ser
430 435 440

CAG CGA TAC AAA CTT GGA GTT CGC TTG TAT TAC CGA GTA ATG GAA TCC 1515
Gln Arg Tyr Lys Leu Gly Val Arg Leu Tyr Tyr Arg Val Met Glu Ser
445 450 455

ATG CTT AAA TCA GAA GAA GAA CGA TTA TCC ATT CAA AAT TTT AGC AAA 1563
Met Leu Lys Ser Glu Glu Glu Arg Leu Ser Ile Gln Asn Phe Ser Lys
460 465 470 475

CTT CTG AAT GAC AAC ATT TTT CAT ATG TCT TTA TTG GCG TGC GCT CTT 1611
Leu Leu Asn Asp Asn Ile Phe His Met Ser Leu Leu Ala Cys Ala Leu
480 485 490

GAG GTT GTA ATG GCC ACA TAT AGC AGA AGT ACA TCT CAG AAT CTT GAT 1659
Glu Val Val Met Ala Thr Tyr Ser Arg Ser Thr Ser Gln Asn Leu Asp
495 500 505

TCT GGA ACA GAT TTG TCT TTC CCA TGG ATT CTG AAT GTG CTT AAT TTA 1707
Ser Gly Thr Asp Leu Ser Phe Pro Trp Ile Leu Asn Val Leu Asn Leu
510 515 520

AAA GCC TTT GAT TTT TAC AAA GTG ATC GAA AGT TTT ATC AAA GCA GAA 1755
Lys Ala Phe Asp Phe Tyr Lys Val Ile Glu Ser Phe Ile Lys Ala Glu
525 530 535

GGC AAC TTG ACA AGA GAA ATG ATA AAA CAT TTA GAA CGA TGT GAA CAT 1803
Gly Asn Leu Thr Arg Glu Met Ile Lys His Leu Glu Arg Cys Glu His
540 545 550 555

CGA ATC ATG GAA TCC CTT GCA TGG CTC TCA GAT TCA CCT TTA TTT GAT 1851
Arg Ile Met Glu Ser Leu Ala Trp Leu Ser Asp Ser Pro Leu Phe Asp
560 565 570

CTT ATT AAA CAA TCA AAG GAC CGA GAA GGA CCA ACT GAT CAC CTT GAA 1899
Leu Ile Lys Gln Ser Lys Asp Arg Glu Gly Pro Thr Asp His Leu Glu
575 580 585

TCT GCT TGT CCT CTT AAT CTT CCT CTC CAG AAT AAT CAC ACT GCA GCA 1947
Ser Ala Cys Pro Leu Asn Leu Pro Leu Gln Asn Asn His Thr Ala Ala
590 595 600

GAT ATG TAT CTT TCT CCT GTA AGA TCT CCA AAG AAA AAA GGT TCA ACT 1995
Asp Met Tyr Leu Ser Pro Val Arg Ser Pro Lys Lys Lys Gly Ser Thr
605 610 615

ACG CGT GTA AAT TCT ACT GCA AAT GCA GAG ACA CAA GCA ACC TCA GCC 2043
Thr Arg Val Asn Ser Thr Ala Asn Ala Glu Thr Gln Ala Thr Ser Ala
620 625 630 635

TTC CAG ACC CAG AAG CCA TTG AAA TCT ACC TCT CTT TCA CTG TTT TAT 2091
Phe Gln Thr Gln Lys Pro Leu Lys Ser Thr Ser Leu Ser Leu Phe Tyr
640 645 650

AAA AAA GTG TAT CGG CTA GCC TAT CTC CGG CTA AAT ACA CTT TGT GAA 2139
Lys Lys Val Tyr Arg Leu Ala Tyr Leu Arg Leu Asn Thr Leu Cys Glu
655 660 665

CGC CTT CTG TCT GAG CAC CCA GAA TTA GAA CAT ATC ATC TGG ACC CTT 2187
Arg Leu Leu Ser Glu His Pro Glu Leu Glu His Ile Ile Trp Thr Leu
670 675 680

TTC CAG CAC ACC CTG CAG AAT GAG TAT GAA CTC ATG AGA GAC AGG CAT 2235
Phe Gln His Thr Leu Gln Asn Glu Tyr Glu Leu Met Arg Asp Arg His
685 690 695

TTG GAC CAA ATT ATG ATG TGT TCC ATG TAT GGC ATA TGC AAA GTG AAG 2283
Leu Asp Gln Ile Met Met Cys Ser Met Tyr Gly Ile Cys Lys Val Lys
700 705 710 715

AAT ATA GAC CTT AAA TTC AAA ATC ATT GTA ACA GCA TAC AAG GAT CTT 2331
Asn Ile Asp Leu Lys Phe Lys Ile Ile Val Thr Ala Tyr Lys Asp Leu
720 725 730

CCT CAT GCT GTT CAG GAG ACA TTC AAA CGT GTT TTG ATC AAA GAA GAG 2379
Pro His Ala Val Gln Glu Thr Phe Lys Arg Val Leu Ile Lys Glu Glu
735 740 745

GAG TAT GAT TCT ATT ATA GTA TTC TAT AAC TCG GTC TTC ATG CAG AGA 2427
Glu Tyr Asp Ser Ile Ile Val Phe Tyr Asn Ser Val Phe Met Gln Arg
750 755 760

~~CTG AAA ACA AAT ATT TTG CAG TAT GCT TCC ACC AGG CCC CCT ACC TTG 2475~~
~~Leu Lys Thr Asn Ile Leu Gln Tyr Ala Ser Thr Arg Pro Pro Thr Leu~~
~~765 770 775~~

~~TCA CCA ATA CCT CAC ATT CCT CGA AGC CCT TAC AAG TTT CCT AGT TCA 2523~~
~~Ser Pro Ile Pro His Ile Pro Arg Ser Pro Tyr Lys Phe Pro Ser Ser~~
~~780 785 790 795~~

~~CCC TTA CGG ATT CCT GGA GGG AAC ATC TAT ATT TCA CCC CTG AAG AGT 2571~~
~~Pro Leu Arg Ile Pro Gly Gly Asn Ile Tyr Ile Ser Pro Leu Lys Ser~~
~~800 805 810~~

~~CCA TAT AAA ATT TCA GAA GGT CTG CCA ACA CCA ACA AAA ATG ACT CCA 2619~~
~~Pro Tyr Lys Ile Ser Glu Gly Leu Pro Thr Pro Thr Lys Met Thr Pro~~
~~815 820 825~~

~~AGA TCA AGA ATC TTA GTA TCA ATT GGT GAA TCA TTC GGG ACT TCT GAG 2667~~
~~Arg Ser Arg Ile Leu Val Ser Ile Gly Glu Ser Phe Gly Thr Ser Glu~~
~~830 835 840~~

~~AAG TTC CAG AAA ATA AAT CAG ATG GTA TGT AAC AGC GAC CGT GTG CTC 2715~~
~~Lys Phe Gln Lys Ile Asn Gln Met Val Cys Asn Ser Asp Arg Val Leu~~
~~845 850 855~~

~~AAA AGA AGT GCT GAA GGA AGC AAC CCT CCT AAA CCA CTG AAA AAA CTA 2763~~
~~Lys Arg Ser Ala Glu Gly Ser Asn Pro Pro Lys Pro Leu Lys Lys Leu~~
~~860 865 870 875~~

~~CGC TTT GAT ATT GAA GGA TCA GAT GAA GCA GAT GGA AGT AAA CAT CTC 2811~~
~~Arg Phe Asp Ile Glu Gly Ser Asp Glu Ala Asp Gly Ser Lys His Leu~~
~~880 885 890~~

~~CCA GGA GAG TCC AAA TTT CAG CAG AAA CTG GCA GAA ATG ACT TCT ACT 2859~~
~~Pro Gly Glu Ser Lys Phe Gln Gln Lys Leu Ala Glu Met Thr Ser Thr~~
~~895 900 905~~

~~CGA ACA CGA ATG CAA AAG CAG AAA ATG AAT GAT AGC ATG GAT ACC TCA 2907~~
~~Arg Thr Arg Met Gln Lys Gln Lys Met Asn Asp Ser Met Asp Thr Ser~~
~~910 915 920~~

~~AAC AAG GAA GAG AAA TGAGGATCTC AGGACCTTGG TGGACACTGT GTACACCTCT 2962~~
~~Asn Lys Glu Glu Lys~~
~~925~~

~~GGATTCATTG TCTCTCACAG ATGTGACTGT AT 2994~~

41. (Original) A method of therapeutically treating inactive, mutative or absent cancer suppressing genes comprising:

treating said inactive, mutative or absent cancer suppressing genes with at least a portion of intact cancer suppressing genes.

42. (Original) A method of claim 41, wherein said cancer suppressing genes are each a substance selected from the groups consisting of RB genes, breast cancer suppressing genes, Wilm's tumor suppressing genes, Beckwith-Wiedemann syndrome suppressing genes, bladder transitional cell carcinoma suppressing genes, neuroblastoma suppressing genes, small cell lung carcinoma suppressing genes, renal cell carcinoma suppressing genes, acoustic neuroma suppressing genes, colorectal carcinoma suppressing genes, and mixtures thereof.

43. (Original) A method of claim 41, wherein said treating includes:

treating said inactive, mutative or absent cancer suppressing gene with a substance selected from the group consisting of an RB gene, a portion of said gene, or a mixture thereof.

44. (Original) A method of claim 43, wherein said portion is selected from the group consisting of RB cDNA, RB cDNA fragment, homologues thereof and mixtures thereof.

45. (Original) The method of claim 41, wherein the intact cancer suppressing gene, or portion thereof, is delivered to the site of a tumor by means of a retrovirus.

46. (Original) A method of claim 41, wherein the intact cancer suppressing gene, or a portion thereof, is delivered to the site of a tumor by a liposome.

47. (Original) A method of claim 41, wherein the location of said cancer suppressing gene is determined by utilizing a genetic marker.

47. (Previously added) A method of suppressing the neoplastic phenotype of a cancer cell, the method comprising contacting the cell with a nucleic acid encoding a full length, wild type retinoblastoma protein.

REMARKS

The amendments to the nucleotide sequence in "TABLE 4" and claims 35 and 40 correct errors of a typographical nature made without deceptive intent. The codons at nucleotide positions 223-225 (CCT), encoding "Pro", and 226-228 (GAG), encoding "Glu", were present in the original sequence from informal Figure 9 of the parent application, 08/472,760, filed November 27,1996, a copy of which is enclosed for the convenience of the Examiner. These codons were inadvertently changed to "CCG" and "TAG" in the present application. That this is inadvertent error is supported by the fact that, under "TAG" at positions 226-228, which encodes a stop codon, the originally-encoded amino acid "E" (Glu) appears in "TABLE 4" of the Specification submitted on December 21, 2001, and "Glu" again appears in the Substitute Specification submitted April 30, 2002, in response to the Notice to File Corrected Application Papers, mailed January 31, 2002.

The Sequence Listing submitted for Application No. 08/472,760, filed November 27,1996, does not contain these inadvertent errors and, thus, the amendments to the Specification and Claims now seek to conform to the nucleotide sequence present in the Sequence Listing of the parent application.

Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. The information contained in the computer readable form of Application No. 08/472,760 was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy, a copy of which is enclosed for the convenience of the Examiner. This amendment contains no new matter.